REMARKS

Claims 182 is amended herewith. Claim 189 is cancelled herein. Accordingly, claims 163-171, 178-188 and 190-195 will be pending.

Supplemental Information Disclosure Statement and Notice Pursuant to M.P.E.P § 2001.06(c)

A Seventh Supplemental Information Disclosure Statement and Notice Pursuant to M.P.E.P § 2001.06(c) is submitted herewith. Applicants respectfully request review and entry of the cited references.

Disclosure Objections

Applicants hereby amend the specification to include the current status of all nonprovisional parent applications referenced. As such, Applicants request withdrawal of the objection.

35 U.S.C. §102 Rejections

Claims 182 and 183

Applicants respectfully request reconsideration of claim 182 as anticipated by U.S. Patent No. 5,709,840 (Juranus '840) or U.S. Patent No. 5,711,917 (Juranus '917).

Amended claim 182 describes a method for parallel processing of reaction mixtures in a combinatorial chemistry reactor system comprising, among other things, pressurizing said vessels to a pressure greater than about 10 psig and introducing a quantity of fluid from a fluid delivery probe into a first vessel of those vessels pressurized according to the pressurizing step. As discussed in the specification, introducing a quantity of fluid into a pressurized vessel "alleviates problems associated with pre-loading vessels with catalysts." (Specification, page 45, line 4). For example, introducing a quantity of fluid under pressure avoids the problems associated with liquid-phase catalytic polymerization of a gaseous monomer, as discussed in detail in the specification. (Specification, page 45, lines 8-23).

More specifically, claim 182 discloses a method for parallel processing of reaction mixtures in a combinatorial chemistry reactor system comprising a plurality of vessels sealed against fluid communication with one another, said method comprising:

(1) providing each of said vessels with one of said reaction mixtures,
(2) pressurizing said vessels to a pressure **greater than about 10 psig,**
(3) **introducing a quantity of fluid from a fluid delivery probe into a first vessel of said plurality of vessels pressurized according to step (2),**

(4) repeating step (3) for a second vessel of said plurality of vessels pressurized according to step (2),
(5) preventing leakage of fluid under pressure from each vessel during and after said introduction of fluid from said fluid delivery probe, and
(6) allowing the reaction mixtures in the vessels to react.

Neither Juranus '840 nor Juranus '917 discloses this novel combination of features. Specifically, neither reference discloses "**pressurizing said vessels to a pressure greater than about 10 psig, [and . . .] introducing a quantity of fluid** from a fluid delivery probe **into a first vessel** of said plurality of vessels **pressurized according to step (2)** . . . ." (emphasis added). Juranus '840 discloses a first embodiment (Figs. 2-4) comprising a reactor cell 30 having an inlet tube 32 sealed with septa 50,52 and a suction (outlet) tube 34 sealed with septa 50,52. Each pair of septa 50,52 is spaced from one another with a corresponding spacer 54, and transverse channel 72 provides communication between such spacers. In order to maintain a sealed environment once either a delivery needle or a sampling needle has punctured a corresponding pair of septa and is removed, a positive pressure of nitrogen gas between 1 and 5 psi (ideally 2 psi) is introduced into the transverse channel, external of the reactor cell 30. The purpose of the channel and positive pressure is to form an anti-leak seal that inhibits the contents of the reactor cell from leaking out a needle hole created in each septa (Juranus '840, column 5, lines 35-50). The second embodiment of Juranus '840 (Fig. 5) similarly discloses a reaction chamber 12 communicating with a septum-sealed inlet and a septum-sealed outlet. This embodiment similarly comprises a transverse channel 72 pressurized to between 1 and 5 psi (ideally 2 psi) to inhibit the contents of the reaction chamber from leaking out a needle hole in each septa. Juranus '917 discloses a similar arrangement with respect to the septum-sealed inlet and outlet and the positive pressure in a transverse channel to inhibit leakage from the reactor vial 12.

Both references fail to disclose pressurizing vessels to a pressure greater than about 10 psig and introducing a quantity of fluid into one of the pressurized vessels, as required by amended claim 182. With the transverse channel 72 pressurized up to 5 psi, transfer of chemical reactants into the reactor may occur at pressures of up to 5 psi. Again, the purpose of such pressurization is to inhibit leakage, rather than to provide injection of reactants into a pressurized environment. Furthermore, because neither reference teaches injection under any pressure greater than approximately 5 psi, and amended claim 182 requires pressurization to a pressure greater than about 10 psig, the references do not anticipate claim amended 182. Applicants respectfully request reconsideration and allowance of claim 182.

Claim 183, which depends directly from claim 182, is submitted as patentable for the same reasons as claim 182.

35 U.S.C. §103 Rejections

Claim 163

Applicants respectfully request reconsideration of claim 163 as obvious in view of U.S. Patent No. 6,045,755 (Lebl), U.S. Patent No. 4,954,149 (Fullemann) and U.S. Patent No. 4,929,614 (Calvet).

Claim 163 describes a combinatorial chemistry reactor apparatus for the parallel processing of reaction mixtures under pressure. Claim 163 further requires an injection system for **introducing fluid into the vessels at pressures different from ambient pressure**. There is no teaching or suggestion in the art of record to combine multiple references – where one discloses parallel processing of reaction mixtures under pressure and another discloses introduction of fluids at pressures different from ambient pressure – where neither reference teaches, suggests or infers such a combination.

Specifically, claim 163 discloses a combinatorial chemistry reactor apparatus for the parallel processing of reaction mixtures under pressure, comprising

> vessels for **containing said reaction mixtures under pressure**, and
> an injection system for **introducing fluid into the vessels at pressures different from ambient pressure**, said injection system comprising:
> a movable fluid delivery probe;
> fill ports for receiving the probe, said probe being movable from one fill port to another to deliver fluid;
> conduits connecting the fill ports and respective vessels;
> valves for opening and closing said conduits, each valve being operable to open to permit the delivery of fluid from the probe to a respective vessel at a pressure different from ambient pressure, and to close before the probe is withdrawn from a respective fill port; and
> seals for maintaining the reaction mixtures under pressure when the valves are open during delivery of fluid from the probe.

(emphasis added).

There is no teaching or suggestion in Lebl or Fullemann to combine the valve of Fullemann with the automated robot teaching of Lebl. Lebl fails to teach or suggest a need for an injection system for introduction of fluids into vessels under pressure. As such, the combination of Lebl and Fullemann is hindsight speculation. Even though Fullemann does teach injection under pressure, there is no teaching, suggestion or inference in Lebl that introduction of fluids under pressure is desirable or would offer an advantage over the disclosed methods and apparatus. Conversely, the teaching in Fullemann for inserting samples into pressurized regions does not teach, suggest or infer that it should be applied to all applications involving pressurized reactions, in particular those that do not explicitly require introduction of a sample under pressure.

More specifically, Fullemann discloses a mechanical septa that "can be used for inserting samples into pressurized regions without leaks due to insertion." (Fullemann, column 8, lines 30-32). However, Lebl fails to disclose a need for a valve capable of introducing fluid into a vessel already at pressure. Lebl provides no teaching or suggestion that introduction of fluids into vessels at pressures other than ambient would be useful. When discussing reactions occurring at pressure, Lebl merely notes that the vessels react at pressure (Lebl, column 25, line 23 to column 26, line 12), but never demonstrates a need for introducing fluid at pressures different from ambient pressure. Rather, Lebl teaches a septum assembly (Figs. 12A and 12B) that includes a central orifice 328 for permitting needle 326 access into the reaction vessel 320 for delivery of fluid and a screw cap 325 that must be screwed down after the needle is removed to seal the central orifice for high temperature/pressure reactions. Because Lebl teaches a two-step operation, (i) fluid delivery followed by (ii) vessel sealing and pressurization, there is no motivation to use the valve of Fullemann with Lebl. Lebl fails to teach or suggest introduction of fluid at pressures different from ambient pressure, and further fails to identify a need for such an introduction. Instead, Lebl teaches delivering reactants to a reaction vessel, then sealing the vessel and only then subjecting the vessel to increased pressure. Because there is no teaching in Lebl or Fullemann for the combination, one skilled in the art would not be motivated to use the Lebl apparatus with the Fullemann seal.

With respect to Examiner's Benzodiazepine argument based upon Calvet, Applicants submit that Calvet teaches away from the claimed invention. In its specification, Lebl notes Benzodiazepine synthesis as an exemplary protocol. (Lebl, column 9, lines 40-54). The Office action cites Calvet to demonstrate that synthesis of Benzodiazepines must occur at elevated pressures, and thus Lebl discloses introduction of fluids into vessels at elevated pressures. As discussed above, Applicants agree that Lebl discloses reactions at elevated pressures. However, disclosing reactions at elevated pressures and disclosing introduction of fluids into reactions at elevated pressures are not the same. Calvet and Lebl both teach the use of reactants at elevated pressures, but neither teaches or suggests anything related to introduction of fluids into a pressurized vessel. Lebl fails to provide such a teaching, as described above. In fact, one of the Calvet examples cited in the Office action teaches away from introduction of fluids under pressure. Example 1 (2nd method) of Calvet discloses the introduction of ruthenium on charcoal under nitrogen into a reactor. (Calvet, column 14, lines 16-29). The ruthenium is hydrogenated for two hours at 10 bars. A second compound is then "added under a nitrogen atmosphere [and t]he reactor is again brought to a hydrogen pressure of 8 bars . . . ." This example clearly demonstrates that both the ruthenium on charcoal and the second compound are added to the reactor under a nitrogen atmosphere, not at elevated pressures, because after introduction, the

reactor is again brought to a hydrogen pressure of 8 bars. Clearly, only after a substance is added does the reactor re-pressurize to an elevated pressure for the reaction to occur. As such, the addition of Calvet teaches away from introduction of fluid into the vessels at pressures different from ambient pressure. For at least the reasons discussed above, Applicants respectfully request reconsideration and allowance of claim 163.

Claims 164-171 and 195, which depend directly or indirectly from claim 163, are submitted as patentable for the same reasons as claim 163.

Commercial Success of Invention

In considering claims 163-171 and 195, the Examiner is requested to take into consideration the fact that the present invention has enjoyed commercial success, having been licensed to The Dow Chemical Company and ExxonMobil, among others. These licenses encompass the use of the apparatus and methodology described in the pending claims of this application. Further, the use of the apparatus and methods of the present invention have achieved excellent results, as demonstrated by the attached pages (marked A-F) taken from a presentation by Dow to a combinatorial materials science conference. It will be noted that page D of the presentation shows Applicant's parallel reactor and refers to exemplary features of significance, including the pressure injection features. The importance of this technology is explained on pages E and F.

The commercial success of the present invention is further evidence of non-obviousness.

Claim 178

Applicants respectfully request reconsideration of claim 178 as obvious in view of Lebl, Fullemann and Calvet.

The apparatus for parallel processing of claim 178 includes a reactor block having a series of wells, a removable plate removably secured to the block, removable liners in the wells and an injection system for introducing fluid into the vessels at pressures different from ambient pressure. The removable plate is removably secured to the reactor block, facing an exterior surface of the reactor block, and has openings therein in registry with the wells in the reactor block. There is no teaching or suggestion in the art of record to include such a removable plate removably secured to a reactor block.

Specifically, claim 178 defines an apparatus for the parallel processing of reaction mixtures, comprising

> a reactor block having a series of wells therein extending down from an exterior surface of the block,

a removable plate removably secured to said reactor block and facing said exterior surface thereof, said removable plate having **openings therein in registry with the wells** in the reactor block,

removable liners in the wells for containing said reaction mixtures under pressure,

an injection system for introducing fluid into the vessels at pressures different from ambient pressure, said injection system comprising:

a movable fluid delivery probe;

fill ports for receiving the probe, said probe being movable from one fill port to another to deliver fluid;

conduits connecting the fill ports and respective wells;

valves for opening and closing said conduits, each valve being operable to open to permit the delivery of fluid from the probe to a respective well at a pressure different from ambient pressure, and to close after said delivery;

stirring mechanisms attached to said removable plate and removable with the plate for stirring said reaction mixtures, said **stirring mechanisms extending through the openings in the removable plate and into respective wells**, and

seals for sealing against leakage through said removable plate openings when the removable plate is secured to the reactor block.

None of the references teaches such a removable plate removably secured to a reactor block and facing an exterior surface thereof, wherein stirring mechanisms are attached to the removable plate and are removable with the plate for stirring the reaction mixtures. None of the references further teaches that the stirring mechanisms extend through the openings in the removable plate and into respective wells. Moreover, the Office action makes no specific reference to a teaching in any reference to each of these relevant features.

In particular, Lebl does not disclose these features. Lebl discloses a base plate 251 having an array of threaded ports for receiving vessels 250. (Lebl, Figs. 10A-10B, column 24, lines 1-38). Another plate 252 sits atop the base plate, cooperating with the base plate to locate and capture an array valve bodies 258 associated with each vessel. Lebl discloses two plates, but fails to disclose the following features of claim 178: (i) a **removable plate removably secured to a reactor block** and facing an exterior surface thereof, (ii) **stirring mechanisms attached to the removable plate** and removable with the plate for stirring the reaction mixtures and (iii) **stirring mechanisms extending through the openings in the removable plate** and into respective wells. Lebl does not teach or suggest a removable plate removably attached to a reactor block. None of the reactor blocks of Lebl is combined with a plate of any kind. Lebl also fails to teach a stirring mechanism of any kind attached to a removable plate. Finally, Lebl discloses no stirring mechanisms extending through openings in a removable plate. Similarly, there is no relevant teaching in either Fullemann or Calvet regarding any of the foregoing

features. Because the references cited in the Office action do not teach the features of claim 178, the combination cannot render claim 178 obvious.

The Office action makes no specific reference within any of the cited references to each of the claimed features. Applicants are therefore unable to ascertain the basis for the present rejection. As such, the Office has not met its burden of establishing a prima facie case of obviousness. Applicants respectfully request that any further rejection of claim 178 be made non-final and include specific recitations of prior art teachings believed to render claim 178 unpatentable.

Claim 179, which depends directly from claim 178, is submitted as patentable for the same reasons as claim 178.

Claim 180

Applicants respectfully request reconsideration of claim 180 as obvious in view of Lebl, Fullemann and Calvet.

Claim 180 describes a method of conducting a catalytic reaction in a plurality of pressurized vessels in a parallel reactor. Among other things, claim 180 allows its reactants to reach equilibrium at a pressure greater than about 10 psig, inserts a fluid delivery probe into one of a plurality of fill ports on the reactor communicating with a first vessel, and injects a quantity of a catalytic fluid from the probe to the first pressurized vessel while maintaining the reactants under pressure. As discussed in detail above with respect to claim 163, Calvet and Lebl both teach the use of reactants at elevated pressures, but neither teaches or suggests anything related to introduction of fluids into a pressurized vessel. Moreover, there is no teaching or suggestion in the art of record to combine multiple references – where one discloses parallel processing of reaction mixtures under pressure and another discloses introduction of fluids at pressures different from ambient pressure – where neither reference teaches, suggests or infers such a combination. Thus, for the reasons discussed above with respect to claim 163, Applicants respectfully request reconsideration and allowance of claim 180.

Claim 181, which depends directly from claim 180, is submitted as patentable for the same reasons as claim 180.

Claim 182

Applicants respectfully request reconsideration of claim 182 as obvious in view of Lebl, Fullemann and Calvet.

Claim 182 describes a method for parallel processing of reaction mixtures in a combinatorial chemistry reactor system comprising a plurality of vessels sealed against fluid

communication with one another. Among other things, claim 182 comprises providing each of the vessels with one of the reaction mixtures, pressurizing the vessels to a pressure greater than about 10 psig and introducing a quantity of fluid from a fluid delivery probe into a first vessel of the plurality of pressurized vessels. As discussed in detail above with respect to claim 163, Calvet and Lebl both teach the use of reactants at elevated pressures, but neither teaches or suggests anything related to introduction of fluids into a pressurized vessel. Moreover, there is no teaching or suggestion in the art of record to combine multiple references – where one, Lebl, discloses parallel processing of reaction mixtures under pressure and another, Fullemann, discloses introduction of fluids at pressures different from ambient pressure – where neither reference teaches, suggests or infers such a combination. Thus, for the reasons discussed above with respect to claim 163, Applicants respectfully request reconsideration and allowance of claim 182.

Claims 183-188 and 190-194, which depend directly or indirectly from claim 182, are submitted as patentable for the same reasons as claim 182.

Applicants request an extension of time to and including August 4, 2003, for filing a response to the above-mentioned Office action. A check in payment of the applicable extension fee of $410 is enclosed.

The Commissioner is requested to charge any other fee deficiency or overpayment in connection with this amendment to Deposit Account No. 19-1345.

Conclusion

In view of the foregoing, Applicants respectfully request reconsideration of the pending claims and issuance of a Notice of Allowance in this case.

Respectfully Submitted,

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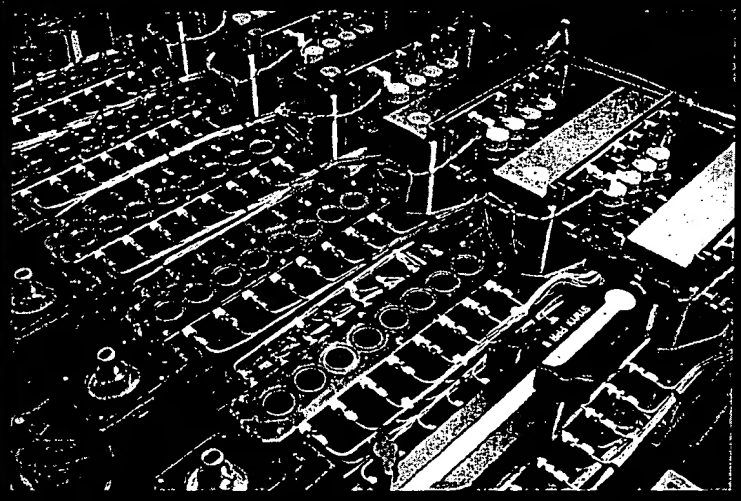

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Catalyst Performance Study: Comments

Data generated by the high throughput tools clearly differentiates catalysts

by understanding the goals that you seek, it is easy to choose the promising candidates for further testing

Combi techniques allowed us to do hundreds of polymerization experiments and gather the polymer data in a tenth of the time required for the conventional approach

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Summary & Conclusions

The use of combinatorial tools is already fundamentally altering our approach to catalyst R&D

The use of the tools themselves allows for extensive and rapid optimization and tuning of current catalysts

Combining these tools with high throughput catalyst synthesis allows us to greatly expand the search for new catalysts, in order to enhance current polyolefin product offerings and develop entirely new products

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